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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,382	08/11/2006	Ferenc Martenyi	PN/4-33153A	3371

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EXAMINER

CHONG, YONG SOO

ART UNIT	PAPER NUMBER
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1617

MAIL DATE	DELIVERY MODE
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06/30/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/550,382	Applicant(s) MARTENYI ET AL.	
	Examiner Yong S. Chong	Art Unit 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 April 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12, 17-19 and 22-25 is/are pending in the application.
- 4a) Of the above claim(s) 19, 23 and 24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12, 17, 18, 22 and 25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>9/21/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's remarks filed on 4/2/09. Claims 22-25 are added. Claims 13-16, 20-21 are cancelled. Claim(s) 1-12, 17-19, 22-25 are pending. Claim(s) 1-2, 7-9, 11-12, 17-19 have been amended. Claim(s) 19 and 23-24 are withdrawn from further consideration as being drawn to a non-elected species. Applicant's election **without traverse** of the restriction requirement in the reply is acknowledged. The requirement is deemed proper and is therefore made FINAL. Claim(s) 1-12, 17-18, 22, 25 are examined herein insofar as they read on the elected invention and species.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham vs John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

Art Unit: 1617

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-12, 22, 25 are rejected under 35 U.S.C. 103(a) as being obvious over Dietrich et al. ("Oxcarbazepine in Affective and Schizoaffective Disorders" *Pharmacopsychiatry*, 2001, 34, 242-250) in view of Almeida et al. ("Safety, Tolerability and Pharmacokinetic Profile of BIA-2-093, a Novel Putative Antiepileptic Agent, during First Administration to Humans," *Drugs R&D* 4(5): pp. 269-284, 2003).

The instant claims are directed to a method of treating manic episodes of bipolar disorder in a patient in need thereof by administering eslicarbazepine acetate.

Dietrich et al. teaches that oxycarbamazepine as well as carbamazepine are effective in the treatment of acute mania and rapid cycling in patients with bipolar affective disorders (pg. 242, right column, Table 1, and conclusion). Concurrent drug treatments with mood-stabilizers and antidepressants are not uncommon in affective disorders (pg. 245, right column, paragraph 2). Dietrich et al. also teach that since oxycarbamazepine does not interact with the cytochrome P450-enzyme system, co-administration with antidepressants might be well-tolerated in affective and schizoaffective disorders (sentence bridging pgs. 247-248). Table 1 shows various dosages of oxycarbamazepine ranging from 500 mg to 2.1 grams per day.

However, Dietrich et al. fail to specifically disclose eslicarbazepine acetate.

Almeida et al. teach that no clinically significant abnormalities in laboratory safety tests, vital signs, weight, physical examination or ECG with BIA 2-093 (also known as eslicarbazepine acetate), therefore considered to be safe and well-tolerated for human

Art Unit: 1617

administration (abstract). BIA 2-093 is derived from carbamazepine and oxcarbazepine since the dibenzazepine nucleus bearing the 5-carboxamide is shared, while structurally different at the 10, 11-position. This molecular variation results in differences in metabolism, namely by preventing the formation of toxic epoxide metabolites and unnecessary production of enantiomers or diastereoisomers of metabolites and conjugates without losing antiepileptic potency (pg. 270, left column, second paragraph and Figure 1).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have substituted eslicarbazepine acetate as taught by Almeida et al, for oxycarbamazepine in the method of treating manic episodes of bipolar disorder as taught by Dietrich et al.

A person of ordinary skill in the art would have been motivated to have substituted eslicarbazepine acetate as taught by Almeida et al, for oxycarbamazepine in the method of treating manic episodes of bipolar disorder as taught by Dietrich et al. because: (1) eslicarbazepine acetate is a derivative of oxycarbamazepine; (2) the functional equivalency of sharing a common structural core; (3) the added benefit of preventing the formation of toxic epoxide metabolites and unnecessary production of enantiomers or diastereoisomers of metabolites and conjugates; and (4) because eslicarbazepine acetate is safe and well-tolerated for human administration. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating manic episodes of bipolar disorder in a patient in need thereof by administering eslicarbazepine acetate in the claimed dosage range.

Art Unit: 1617

Claim(s) 17-18 are rejected under 35 U.S.C. 103(a) as being obvious over Dietrich et al. ("Oxcarbazepine in Affective and Schizoaffective Disorders" *Pharmacopsychiatry*, 2001, 34, 242-250) and Almeida et al. ("Safety, Tolerability and Pharmacokinetic Profile of BIA-2-093, a Novel Putative Antiepileptic Agent, during First Administration to Humans," *Drugs R&D* 4(5): pp. 269-284, 2003) as applied to claims 1-12, 22, 25 in view of Beasley et al. (US Patent 5,605,897).

The instant claims are directed to a method of treating manic episodes of bipolar disorder in a patient in need thereof by administering eslicarbazepine acetate and olanzapine.

Dietrich and Almeida et al. teach as discussed above, however, fail to disclose olanzapine.

Beasley et al. teach the olanzapine is useful in the treatment of bipolar disorder.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have combined olanzapine as taught by Beasley et al. with eslicarbazepine acetate in the method of treating manic episodes of bipolar disorder as taught by Dietrich and Almeida et al.

A person of ordinary skill in the art would have been motivated to combine olanzapine as taught by Beasley et al. with eslicarbazepine acetate in the method of treating manic episodes of bipolar disorder as taught by Dietrich and Almeida et al. because both olanzapine and eslicarbazepine acetate are useful for treating bipolar disorder.

Art Unit: 1617

"It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... The idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Application/Control Number: 10/550,382

Page 7

Art Unit: 1617

/Yong S. Chong/

Primary Examiner, Art Unit 1617

YSC